**Template Investigator Initiated Clinical Study January 2019 (including ECTR clause for implementation local feasibility) – the Netherlands**

**Clinical Study Site Agreement**

(*Template agreement for investigator initiated clinical studies with human subjects, conducted in the Netherlands by academic (NFU) and non-academic (STZ) hospitals and NKI/AvL*)

**Scope of use:**

This template clinical study agreement is created in joint cooperation between the University Medical Center’s (UMC’s) in The Netherlands, supported by the Nationale Federatie van Universitair Medische Centra (NFU); the Vereniging STZ (Samenwerkende Topklinische opleidingsZiekenhuizen) on behalf of STZ-hospitals; and the Stichting Het Nederlands Kanker Instituut - Antoni van Leeuwenhoek Ziekenhuis (NKI/AvL).

The creation and use of this template is supported and endorsed by the Dutch Clinical Research Foundation (DCRF).

This template can be modified as agreed upon between the Parties for accommodating the correct party structure, study-specific requirements, financial arrangements or any other terms and conditions which are relevant for the purpose of the collaboration. During the negotiations any modifications should be marked and explained.

Clinical Study: [*insert title*]

Protocol: [*insert EUDRACT number or Dutch Registration NL-number, date and version number*]

Sponsor (“verrichter”): [*insert name legal sponsor of the clinical study*]

Study Drug/Equipment (if applicable): [*insert name drug or equipment*]

Funder: [*insert name financing party and/or party providing the study drugs*]

Target: [*insert estimated number of Clinical Study Subjects for Study Site inclusion*]

The undersigned,

1. [*insert name of the sponsor institution*], located at [*insert registered address*], duly represented by [*insert name(s) and function(s)*]

(hereinafter referred to as “**Sponsor**”)

and

1. [*insert name of the site institution*], located at [*insert registered address*], duly represented by [*insert name(s) and function(s)*]

(hereinafter referred to as “**Study Site**”)

[N.B. In case a “medisch specialistisch bedrijf” will cosign the Agreement, the following text can be used for the Study Site (**party B**):]

“ [*Name of the hospital*], located at [*registered address*], the Netherlands, duly represented by [*name and function*] (hereinafter referred to as “[*name of hospital*]”; and

[*name of medisch specialistisch bedrijf*], located at [*registered address*], the Netherlands, duly represented by [*name and function*] (hereinafter referred to as “[*name of MSB*]”;

(hereinafter [*name of hospital*] and [*name of MSB*] are jointly referred to as “**Study Site**”)”

**[In case the Site Investigator is not an employee of Study Site and acts as a separate Party:]**

and

1. [*INVESTIGATOR insert: name of physician …», …[function], [tax/office address and chamber of commerce registration number, if applicable*], (hereinafter referred to as “**Site Investigator**”) ]

**[ OR in case the Site Investigator is an employee of the Study Site and not a separate Party: ]**

in the presence of:

Study Site’s employee, [*insert name of physician*]

(hereinafter referred to as “**Site** **Investigator**”)

WHEREAS,

* the Parties each are involved in patient care, research and education;
* the Sponsor [if applicable: and Study Site jointly] and in particular ………………………… (hereinafter the “**Principal** **Investigator**”), researcher employed by Sponsor who has designed the Clinical Study identified hereof;
* **[if applicable**: this Clinical Study is financially and/or in-kind supported by ………………………(hereinafter: the “**Funder**”) by means of a clinical study grant provided to Sponsor under Funder’s grant terms which are, in whole or in part, annexed hereto as Annex 3 if and to the extent applicable to Study Site;
* the Study Site has facilities and personnel with the requisite skills, experience, and knowledge required to support the performance of the Clinical Study by the Site Investigator;
* the Sponsor wishes to engage the Study Site and Site Investigator to perform part of the Clinical Study and Site Investigator and Study Site, having reviewed the Protocol and relevant Clinical Study information, is willing to participate in the Clinical Study.

In consideration of the undertakings and commitments set forth herein, the Parties agree to enter into this Clinical Study Site Agreement.

1. **DEFINITIONS**

The following words and phrases have the following meanings:

* + 1. “**Affiliate**” means any business entity which controls, is controlled by, or is under the common control of, a Party. For the purposes of this definition, a business entity shall be deemed to control another business entity if it owns, directly or indirectly, in excess of 50% of the voting interest in such business entity or the power to direct the management of such business entity or to elect or appoint 50% or more of the members of the management of such business entity;
    2. “**Agreement**” means this agreement comprising its recitals, clauses, schedules and any annexes attached hereto, including the Protocol and including any written amendments to the Agreement agreed between the Parties;
    3. “**Auditor**” means a person who is authorised by Sponsor and/or Funder to carry out a systematic review and independent examination of clinical study related activities and documents to determine whether the evaluated Clinical Study related activities were conducted, and the data were recorded, analysed and accurately reported according to the Protocol, (if applicable) the standard operating procedures of Sponsor, ICH-GCP and the applicable regulatory requirements;
    4. “**Authorisation**” means the authorisation of a clinical study, or any protocol amendments, in accordance with article 2, and (if applicable) 13i and 13k, of the Dutch *Medical Research Involving Human Subjects Act*;
    5. “**CCMO**” means the Dutch clinical trial authority, namely the Central Committee on Research involving Human Subjects (in Dutch: “Centrale Commissie Mensgebonden Onderzoek” or “CCMO”);
    6. “**Clinical Study**” means the investigation as defined in the cadre above, (also) to be conducted at the Study Site in accordance with the Protocol;
    7. “**Clinical Study Subject**” means a person enrolled to participate in the Clinical Study;
    8. “**Competent Authority**” means the authority appointed to evaluate the Clinical Study in accordance with 13i of the Dutch *Medical Research Involving Humans Subjects Act*, based on article 9 of the European Clinical Study Directive 2001/20/EC;
    9. “**Confidential Information**” means any and all information, data and material of any nature belonging or entrusted to a Party and/or its Affiliate(s), or which is a trade secret, which such Party (the “**Disclosing Party**”) may disclose in any form to the other Parties (each a “**Receiving Party**”) pursuant to this Agreement, the release of which is likely to prejudice the interests of the Disclosing Party;
    10. “**CRF**” means the case report form in a format prepared by Sponsor and documenting the administration of the Investigational Product (if applicable) to Clinical Study Subjects as well as all tests and observations related to the Clinical Study and “**eCRF**” means a CRF in electronic form;
    11. “**Effective Date**” the date this Agreement comes into effect, being the date of the last Party’s signature to this Agreement;
    12. “**Ethics Committee**” means the accredited medical research ethics committee competent to review the Clinical Study in accordance with applicable Law, and to which the Protocol has been submitted for approval;
    13. “**GDPR**” means Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation);
    14. **“ICF”** means the Informed Consent Form as approved by the Ethics Committee, in which the Clinical Study Subject consents to his participation in the Clinical Study, including a consent, as defined in article 4 paragraph 11 of the GDPR, regarding the processing of the Clinical Study Subject’s Personal Data which shall meet the requirements relating thereto of the GDPR;
    15. “**ICH-GCP**” means the ICH Harmonised Tripartite Guideline for Good Clinical Practice (CPMP/ICH/135/95 together with such other good clinical practice requirements as are specified in Directives 2001/20/EC and 2005/28/EC of the European Parliament and the Council relating to medicinal products for human use and in guidance published by the European Commission pursuant to such Directives;
    16. “**Independent Committee**” means a committee such as a Data and Safety Monitoring Board (“DSMB”), which is a group of individuals with pertinent expertise that have oversight of and reviews on a regular basis accumulating data from one or more ongoing clinical studies and that advise the Sponsor regarding the continuing safety of Clinical Study Subjects and those to be recruited to the Clinical Study, as well as the continuing validity and scientific merit of the Clinical Study;
    17. “**Intellectual Property Rights**” means intellectual property rights including but not limited to patents, trade-marks, trade names, service marks, copyrights, rights in and to databases (including rights to prevent the extraction or reutilisation of information from a database), design rights, topography rights and all rights or forms of protection of a similar nature or having equivalent or the similar effect to any of them which may subsist anywhere in the world, whether or not any of them are registered and including applications for registration of any of them;
    18. “**Investigational Product**” means the Study Drug and the control material, as further detailed in the Protocol;
    19. “**Know How**” means all technical and other information which is not in the public domain (other than as a result of a breach of confidence), including but not limited to information comprising or relating to concepts, discoveries, data, designs, formulae, ideas, inventions, methods, models, procedures, designs for experiments and tests and results of experimentation and testing, processes, specifications and techniques, laboratory records, manufacturing data and information contained in submissions to regulatory authorities, whether or not protected by Intellectual Property Rights;
    20. “**Law**” means any international, European Union and Dutch law and regulations, as well as generally accepted international conventions applicable to the performance of the Clinical Study. Such Law including but not limited to:
* Directives 2001/20/EC and 2005/28/EC of the European Parliament and the Council relating to medicinal products for human use and in guidance published by the European Commission pursuant to such Directives and any implementation in Study Site’s national Law (if applicable)
* the Dutch Medical Research Involving Human Subjects Act (*Wet Medisch-wetenschappelijk Onderzoek met Mensen or WMO*),
* the GDPR, and any applicable national implementing legislation,
* the Dutch Medical Treatment Agreements Act (*Wet op de geneeskundige behandelingsovereenkomst* or *Wgbo*),
* the ICH-GCP,
* the directives on “the assessment of Clinical Trial Agreements (2011)” and on “External Review 2012)” issued by the CCMO,
* the principles of the Dutch Code of Conduct regarding the adequate procurement, management and use of bodily human tissue published by the Federation of Dutch Medical Scientific Societies,
* the Declaration of Helsinki, the most recent version,
* and/or any successors of the above mentioned Laws.
  + 1. “**Party**” means the Sponsor or the Study Site or, *only if the Site Investigator is a separate Party to this Agreement*, the Site Investigator, and “**Parties**” shall mean the two or all of them jointly;
    2. “**Personal Data**” means personal data as defined in article 4(1) of the GDPR, i.e. any information relating to an identified or identifiable natural person, e.g. such information of a Clinical Study Subject;
    3. “**Protocol**” means the document as defined in the cadre at the beginning of this Agreement, detailing all aspects of the Clinical Study, and for which Authorisation has been obtained, a copy of which is attached as Annex 1 to this Agreement. The Protocol includes all amendments thereto for which Authorisation has been obtained;
    4. “**Research Staff**” means the person(s) who will undertake the conduct of the Clinical Study at the Study Site on behalf of the Site Investigator and under the supervision of the Site Investigator;
    5. “**Samples**” means any human biological materials, including but not limited to blood, body tissue, plasma and any other material containing human cells;
    6. “**Site Investigator**” means the person who will take primary responsibility for the conduct of the Clinical Study at the Study Site or any other person as may be agreed from time to time between the Parties as a replacement;
    7. **“Site Parties”** mean the Study Site and Site Investigator jointly;
    8. “**Study Drug**” means the study drug that is object of investigation and which is to be used by Site Parties in accordance with the Protocol;
    9. “**Study Monitor**” means one or more persons appointed by the Sponsor to monitor compliance of the Clinical Study with ICH-GCP and the Protocol and to conduct source data verification;
    10. “**Target**” means the estimated number of Clinical Study Subjects to be included in the Clinical Study as referred to in the cadre above.

1. **OBLIGATIONS** 
   1. The Parties agree to perform the Clinical Study in accordance with the Protocol, this Agreement and applicable Law.
   2. The Parties represent and warrant that they each have the authority to enter into this Agreement. In case the Site Investigator is not a Party to this Agreement, Study Site shall ensure the performance of the tasks assigned to the Site Investigator under this Agreement and by no means will the Site Investigator be held liable hereunder in person in the event that he/she is not a Party to this Agreement. The Study Site will ensure the availability of and/or access to any resources necessary to perform the Clinical Study at the Study Site, including departments, facilities and Research Staff and support personnel, and the Study Site certifies (in Dutch: “verklaart”) that the Site Investigator holds the necessary registration and has the necessary qualifications, expertise and time to perform the Clinical Study.
   3. The Study Site shall notify the Sponsor if the Site Investigator ceases to be associated with the Study Site where the Clinical Study will be conducted or if he/she is otherwise unavailable to continue as Site Investigator, and Study Site shall use all reasonable endeavours to find a qualified successor acceptable to the Sponsor. Replacement of the Site Investigator is subject to authorisation by the Ethics Committee. If subject to the foregoing no mutually acceptable replacement can be found, within reasonable time as not to hinder the safe continuation of the Clinical Study at the Study Site, and provided that the Sponsor will not unreasonably withhold its approval of the proposed replacement of Site Investigator, each Party may terminate this Agreement pursuant to clause 11.2.g below.
2. **CLINICAL STUDY GOVERNANCE AND COMPLIANCE**
   1. The Sponsor shall be responsible for obtaining and maintaining Authorisation for the Clinical Study and (substantial) amendments to the Protocol.
   2. In the event of any substantial amendments being made to the Protocol, the amendments shall be signed by the Site Investigator and shall be implemented after Authorisation and a favourable opinion of the Ethics Committee. The Site Investigator shall not consent to any change in the Protocol requested by the Ethics Committee or Competent Authority without the prior written consent of the Sponsor.
   3. The Clinical Study shall be performed at the Study Site. The Site Investigator shall be responsible for obtaining permission (in Dutch: “onderzoeksverklaring”) from the representatives of the Study Site to perform the Clinical Study at the Study Site, which shall include the engagement of the Research Staff and, to the extent applicable, other departments.
   4. The Sponsor shall be responsible for submitting the Clinical Study for listing on a free, publicly accessible clinical study registry.
   5. The Site Investigator shall submit CRF/eCRFs to the Sponsor as outlined in the Protocol.
   6. The Site Parties shall make and retain records regarding the Clinical Study as required by the Protocol, applicable Law, and in accordance with the Study Site’s standard archiving procedures. Site Parties will retain such records for the minimum period of time required under applicable Law. If indicated by Sponsor that such is reasonably required for regulatory purposes, Site Parties shall retain the records for a longer period of time, and to the extent applicable, at Sponsor’s expense.
3. **LIABILITIES, INDEMNIFICATION AND INSURANCE**
   1. Sponsor shall arrange insurance cover in respect of its potential liability for damages to Clinical Study Subjects resulting from the Clinical Study in accordance with the requirements set out in the WMO and the Decree on Obligatory Insurance for Medical Studies involving Human Subjects of 1 July 2015, unless this requirement has been waived by the Ethics Committee, in which case the indemnification obligations of Sponsor under this clause 4 shall not apply and Parties shall be entirely liable for their own actions, including those of any and all of their employees, students, agents and Affiliates hereunder.
   2. Subject to the limitations set out hereinafter, and without prejudice to clause 4.1 above, Sponsor, being the insurance holder as set out in clause 4.1 above, shall indemnify (in Dutch: “schadeloosstellen”) and hold harmless (in Dutch: “vrijwaren”) Study Site, its employees, the Site Investigator and the Research Staff (the “**Indemnitees**”) against all claims, demands, actions or proceedings (to include any settlements or ex gratia payments made with the consent of the Parties hereto and reasonable legal and expert costs and expenses) made or brought (whether successfully or otherwise): (i) by or on behalf of any Clinical Study Subject for personal injury or death arising out of the administration or use of the Investigational Product during or as a result of the Clinical Study, or (ii) of any clinical intervention or procedure provided for or required by the Protocol, to which the Clinical Study Subject would not have been exposed but for its participation in the Clinical Study.
   3. Without prejudice to clause 4.1 above, Sponsor’s indemnification and defence of the Indemnitees shall not apply to any claim or proceeding pursuant to clause 4.2, and Sponsor shall not be liable:

(a) to the extent that said personal injury (including death) is caused by any of the Indemnitees’ failure to comply with this Agreement or the Protocol; or

(b) to the extent that said personal injury (including death) is caused by gross negligence, wilful recklessness or wilful conduct or wilful misconduct (in Dutch: "bewuste roekeloosheid of opzettelijk handelen of nalaten*”*) of any of the Indemnitees.

* 1. Parties shall keep each other reasonably informed of developments in relation to any such claim or proceeding. Parties will consult with each other on the nature of any defence to be advanced.
  2. Parties will each give to the other such help as may reasonably be required for the efficient conduct and prompt handling of any claim or proceeding made or brought by or on behalf of Clinical Study Subjects (or their dependants).
  3. Except in the event of intentional behaviour or gross negligence of a Party, in no event will a Party’s liability towards the other Party include any indirect damages (indirect damages meaning: loss of profit, loss of revenue and loss of business opportunities).
  4. The aggregate liability of the Site Parties for a claim or proceeding of Sponsor under this Agreement shall be limited to EUR 500.000, except and to the extent such claim or proceeding is made for damages caused by: **A)** gross negligence, wilful recklessness or wilful conduct or wilful misconduct (in Dutch: "bewuste roekeloosheid of opzettelijk handelen of nalaten”) of any of the Site Parties and cannot be so restricted or excluded by Law, or **B)** claims or proceedings between the Parties arising from the joint and several liability in connection with the joint controllership of the Parties under the GDPR as further laid down in clause 7 below.
  5. Parties shall take out and/or maintain an insurance cover, or have a system of self-insurance in place, in amounts sufficient to cover their potential liability under this Agreement.

1. **CLINICAL STUDY SUBJECT RECRUITMENT AND ENROLLMENT**
   1. The Site Parties shall use reasonable endeavours to recruit the Target of Clinical Study Subjects to the Clinical Study as indicated in the cadre above. Site Investigator shall make sure that the Clinical Study Subjects (and/or their legal representatives, if applicable) will, in accordance with applicable Law, be duly informed prior to their participation in the Clinical Study, in a language the Clinical Study Subjects (and/or their legal representatives, if applicable) can fully understand on all aspects of the Clinical Study which are deemed relevant in their decision to participate, and give informed consent. Site Investigator shall inform each Clinical Study Subject of the collection, the use and the transfer of Personal Data and the Clinical Study Subjects rights in respect of such processing as set forth in articles 13 and 14 GDPR, as well as the essence of the arrangement between the Parties as joint controllers referred to in article 26 paragraph 1 GDPR.
   2. If circumstances or events have occurred or will occur that will substantially delay or are likely to substantially delay the progress of recruitment or enrolment of the Clinical Study Subjects, the Site Investigator shall without undue delay inform the Sponsor in writing. In each such event Parties shall discuss the consequences of the delay and each Party shall undertake reasonable endeavours to agree on measures to handle the delay.
   3. In the event that the Clinical Study is part of a multi-centre clinical study, the Site Investigator acknowledges and agrees that recruitment may be competitive and that Sponsor may stop further recruitment of Clinical Study Subjects at the Study Site when the recruitment target for all investigational sites for this Clinical Study has been met, even if the Study Site has not yet recruited the Target.
2. **QUALITY ASSURANCE AND CONTROL**
   1. The Site Parties shall permit the Study Monitor, Auditor and any official with a legal right to inspect and access all relevant documentation and source data for monitoring of the progress of the Clinical Study, the proper collection and recording of Clinical Study data, the welfare of the Clinical Study Subjects, and altogether the good quality of the Clinical Study and compliance with applicable Law and, if applicable and communicated to the Site Parties in writing, Sponsor’s standard operating procedures. The Study Monitor and Auditor’s access will be arranged at mutually convenient times and on reasonable notice with no additional costs for the Study Monitor, Auditor or Sponsor. The Study Monitor and Auditor will comply with all internal policies and regulations of the Site Parties during such inspection, to the extent these are sufficiently communicated to the Study Monitor or Auditor. For the avoidance of any doubt, the Sponsor shall be responsible for the confidential handling of all Personal Data of Clinical Study Subjects and other patients which the Study Monitor or Auditor comes across with during their monitoring or auditing activities. Before the start of the monitoring or auditing visits, the Sponsor shall provide the Site Parties with the name of the appointed Study Monitor or auditor, and hereby warrants (in Dutch: “staat garant”) that such Study Monitor or Auditor shall timely sign a confidentiality statement regarding the above by means of a specific letter. of the template for such letter is annexed to this Agreement below, as Annex 4.
   2. The Site Parties shall promptly inform the Sponsor in writing of any intended or actual inspection, written enquiry and/or visit to the Site Parties by any regulatory authority in connection with the Clinical Study and forward to the Sponsor copies of any correspondence from any such regulatory authority relating to the Clinical Study. The Site Parties shall allow Sponsor’s representatives to be present during any such visit.
   3. The Site Parties shall take appropriate measures and/or corrective actionswithout delay as the Sponsor may reasonably require in order to solve all problems found and reported by the Study Monitors, Auditor or officers from regulatory authorities or during an inspection under clause 6.2.
   4. The Site Parties shall permit authorized representatives of the Ethics Committee and Competent Authorities to have access to and verify information relating to the Clinical Study, as required by and in accordance with applicable Law. Parties acknowledge that the Clinical Study is subject to inspection by regulatory authorities worldwide and that such inspections may occur after the completion of the Clinical Study.
   5. It is expressly agreed between the Parties that:
3. the Sponsor will not compensate the Site Investigator nor any member of the Research Staff for the assistance or guidance of representatives of the Ethics Committee, Competent Authority or other regulatory authority and
4. the assistance or guidance of Study Monitors or Sponsor’s Auditors by the Site Investigator and the Research Staff shall not be compensated by Sponsor, unless expressly agreed otherwise in writing.
5. **CONFIDENTIALITY AND DATA PROTECTION**

*Confidential Information*

* 1. The Receiving Party shall ensure that only those of its officers and employees concerned with the carrying out of this Agreement have access to the Confidential Information of the Disclosing Party. The Receiving Party shall take all practicable steps to ensure that such persons abide by the same obligations of confidentiality as apply to the Receiving Party under this Agreement. The Receiving Party undertakes to treat as strictly confidential and not to disclose to any third party any Confidential Information of the Disclosing Party, except where disclosure is required by a regulatory authority or by law, in which case the Receiving Party shall inform the Disclosing Party in writing of such requirement and the information to be disclosed. Notification will be within a reasonable time prior to being required to make the disclosure or if such time is not available, immediately upon becoming known of the requirement to disclose, Confidential Information. The Receiving Party undertakes not to make use of any Confidential Information of the Disclosing Party, other than in accordance with this Agreement, without the prior written consent of the Disclosing Party. For purposes of this Agreement and subject to clause 10 (Publication and Authorship), the Clinical Study results generated by Site Parties as disclosed through the CRF shall be considered Confidential Information of Sponsor and this clause 7 shall not provide Site Parties the rights granted hereunder to the Disclosing Party, where it relates to such Clinical Study results owned by Sponsor.
  2. The obligations of confidentiality and non-use set out in clause 7.1 shall not apply to information which the Receiving Party can show by competent evidence:
     1. is or becomes part of the public domain by any other means than a wrongful act or breach of this Agreement by the Receiving Party;
     2. was or becomes in the Receiving Parties’ lawful possession prior to the disclosure without restriction on disclosure;
     3. has been independently developed by the Receiving Party without the use of Confidential Information of the Disclosing Party;
     4. has been obtained by the Receiving Party from a third party without breach of a confidentiality obligation; or
     5. is published in accordance with clause 10 hereof.

*Medical confidentiality, data protection and data controlling*

* 1. In line with the current position of the CCMO, the Study Site and Sponsor are considered joint controllers for the processing of the Personal Data and will both handle all Personal Data in accordance with the GDPR and any other to the performance of the Clinical Study applicable laws or regulations covering the protection of Personal Data (collectively “**Data Protection Law**”). Parties, will fully cooperate with each other as joint controllers and shall take the necessary measures in order to comply with the Data Protection Law, such cooperation shall duly reflect the respective roles and relationships of the joint controllers vis-à-vis the Clinical Study Subjects as data subjects, in particular as regards the exercising of the rights of these data subjects and the Parties’ respective duties to provide the information referred to in Articles 13 and 14 of the GDPR. Each joint controller shall maintain a record of processing activities under its responsibility.

*In the event law and interpretation by the CCMO and/or a relevant data protection authority or a court decision should prescribe or indicate another qualification of the roles of the parties in clinical trial agreements, the Parties hereto shall consult with each other and shall adapt the qualification of their roles and change arrangements as may be deemed appropriate.*

* 1. Each Party shall be responsible for its own processing of Personal Data in accordance with all Data Protection Law and with the ICFs obtained from Clinical Study Subjects and to the extent applicable, Personal Data consents obtained from the Site Investigator and Research Staff.
  2. Both Sponsor and Study Site shall implement appropriate technical and organizational measures to meet the requirements of the GDPR.
  3. If any Party becomes aware of a Personal Data breach in connection with this Clinical Study or the performance of this Agreement, that Party shall promptly notify the other Party/-ies, and, the Party that is the controller of the relevant Personal Data shall also document the Personal Data breach and report the breach to the applicable regulatory authorities. In such case, Parties will fully cooperate with each other in order to fulfil the (statutory) notification obligations timely. A Personal Data breach refers to: a personal data breach as defined in article 4 paragraph 12 GDPR and further determined by articles 33 and 34 of the GDPR.
  4. Each Party agrees to co-operate with any competent supervisory authority and to allow such supervisory authority to audit each Party’s compliance with the GDPR.
  5. The Parties agree to adhere to the principles of medical confidentiality in relation to Clinical Study Subjects.
  6. Sponsor shall provide an Ethics Committee approved ICF to Site Parties.
  7. Sponsor acknowledges that Clinical Study Subjects – and/or their legal representatives on their behalf – may withdraw, in whole or in part, their initial informed consent. Site Investigator shall promptly notify Sponsor of any such withdrawal of the informed consent of a Clinical Study Subject, which may affect the use of such Clinical Study Subject’s Personal Data under this Agreement. The Site Investigator will communicate with Sponsor on behalf of the Clinical Study Subject. However, the procedure followed upon such withdrawal of a Clinical Study Subject’s consent will be according to the instructions, to the extent laid down in the Protocol and the ICF, and in accordance with the Aplicable(Data Protection) Law.
  8. Sponsor shall refrain from tracing and/or identifying any Clinical Study Subject, except where Sponsor is under a legal obligation to do so. In the event any Clinical Study Subject, for any other than aforementioned reason, becomes identifiable to Sponsor, Sponsor agrees to preserve, at all times, the confidentiality of information pertaining to such Clinical Study Subjects.

*Site Investigator’s (and Research Staff’s) personal information*

* 1. Where applicable, Sponsor shall inform the Site Investigator, and to the extent applicable other Research Staff involved in the Clinical Study as well, of the collection, the use and the transfer of his/her/their Personal Data and his/her/their rights in respect of such processing as set forth in articles 13 and 14 GDPR, as well as the essence of the arrangement between the Parties as joint controllers referred to in article 26 paragraph 1 GDPR. Site Parties agree to help Sponsor obtain any express consents, as may be necessary in accordance with applicable Data Protection Law from the Site Investigator, and to the extent applicable and necessary from other Research Staff involved in the Clinical Study as well, for any intended processing of his/her/their Personal Data by Sponsor.

1. **INTELLECTUAL PROPERTY**
   1. All Intellectual Property Rights and Know How owned by or licensed to any of the Parties prior to and after the date of this Agreement, other than any Intellectual Property Rights and Know How arising from the Clinical Study, are and shall not be affected by this Agreement.
   2. [**or A**]The Sponsor shall own the Intellectual Property Rights and Know How arising from and directly relating to the Clinical Study and the Protocol, but excluding (1) any clinical procedure and improvements thereto that are clinical procedures of the Site Investigator or of Study Site (2) any patient medical records and (3) copyrights on work published by the Site Investigator in accordance with clause 10 hereinafter, which copyrights shall either vest in the Study Site or, if made by the Site Investigator and other authors, in the Study Site and the other co-author(s) in accordance with applicable copyright laws or as mutually agreed between the Parties, or shall vest in the publisher of such work upon the transfer of copyrights by the author(s).

[**or B**] The Parties shall jointly own the Intellectual Property Rights and Know How arising directly from the Clinical Study (“**Joint IP**”).

* 1. The Site Investigator will promptly inform the Sponsor of any invention or discovery arising from and directly relating to the Clinical Study, , and Study Site hereby assigns rights in relation to all Intellectual Property Rights in relation to such invention or discovery, and will provide reasonable assistance to the Sponsor in filing or prosecuting Intellectual Property Rights, at the expense of the Sponsor.
  2. Nothing in this clause 8 shall be construed so as to prevent or hinder the Site Parties from using the Know How generated during their conduct of the Clinical Study for their normal hospital, non-commercial research and education activities, , to the extent such use does not result in the disclosure or misuse of Confidential Information or the infringement of any Intellectual Property Rights of the Sponsor.
  3. [**if B under 8.2**] *Protection, maintenance and costs of Joint IP:* After completion of the Clinical Study at all participating sites the Parties shall make additional arrangements with regard to application, acquisition and/or maintenance of the Joint IP. The Sponsor is designated as lead party therein.

Site Parties understand and agree that other participating sites may also have a right to the Joint IP. Sponsor shall ensure that such other participating sites adhere to the same terms and conditions with regards to Joint IP as Site Parties.

Sponsor shall timely discuss with the other participating sites any intended applications, reports etc. related to the Joint IP in order to give the other participating sites the opportunity to comment there on.

Each Party shall, and shall ensure that its employees, researchers, research fellows, individuals equivalent to those persons, give full cooperation and shall execute all documents, deeds and so forth as may reasonably be required in connection with the registration, protection and/or maintenance of that Joint IP.

* 1. In case Sponsor has an agreement on Intellectual Property Rights with a Funder, that agreement shall prevail over this clause 8 in case of conflict. In such case, Sponsor shall be obliged to fully inform the Study Site on all relevant aspects of such agreement within reasonable time prior to the execution of this Agreement.
  2. In case a third party brings a claim or initiates proceedings against the Site Parties for the use of Intellectual Property Rights owned by or provided through Sponsor in conducting the Clinical Study in accordance with this Agreement, Sponsor shall indemnify the Site Parties against such claims or proceedings, provided the Site Parties shall have notified Sponsor promptly in writing of it and shall, upon Sponsor’s request and at Sponsor’s costs, have permitted Sponsor to have full control and discretion over the claim or proceeding using legal representation of its own choosing under the same conditions as set forth in clause 4.5-4.6.

1. **PUBLICITY**
   1. The Sponsor will not use the logo or name of the Study Site, Site Investigator, nor of any member of the Research Staff, for promotional purposes, in any publicity, advertising or news release without the prior written approval on a case-by-case basis of the Study Site or Site Investigator, such approval not to be unreasonably withheld. The Study Site and Site Investigator will not, and will ensure that the Research Staff will not, use the name or logo of the Sponsor or of any of its employees for promotional purposes, in any publicity, advertising or news release without the prior written approval of the Sponsor on a case-by-case basis, such approval not to be unreasonably withheld.
   2. The Site Parties will not issue and will ensure the Research Staff will not issue any information or statement to the press or public, including but not limited to advertisements for the enrolment of Clinical Study Subjects, without, where appropriate, the review and the issue of a favourable decision from the Ethics Committee and the prior written permission of the Sponsor.
2. **PUBLICATION AND AUTHORSHIP**

*Principles and multi-centre publication*

* 1. The Sponsor, Study Site and the Site Investigator each acknowledge the importance of public disclosure/publication of information collected or generated as a result of or related to the Clinical Study, under the condition that public disclosure/publication takes place under the provisions of this clause 10.
  2. Upon completion of the Clinical Study (whether prematurely or otherwise) the Site Investigator and Sponsor may co-operate in producing a report of the Clinical Study detailing the methodology, results and containing an analysis of the results and drawing appropriate conclusions.
  3. As the Clinical Study is a multi-centre study, any publication based on the results obtained at the Study Site (or a group of sites) shall not be made before the first multi-centre publication or presentation, which shall be coordinated by Sponsor, unless otherwise agreed in writing, or as provided for in this clause 10. Notwithstanding the foregoing, if a multi-centre publication is not published within twelve (12) months after completion of the Clinical Study and lock of the Clinical Study database at all research sites that are part of the multi-centre Clinical Study or any earlier termination or abandonment of the Clinical Study, the Site Investigator and/or members of the Research Staff shall have the right to publish or present the methods and results of the Clinical Study in accordance with the provisions of this clause 10.

*Publications by Site Investigator*

* 1. Subject to clause 10.3 above, the Sponsor agrees that the Site Investigator and/or members of the Research Staff shall be permitted to present at symposia, national or regional professional meetings, and to publish in journals, theses or dissertations, or otherwise of its own choosing, methods and results of the Clinical Study, subject to the terms of this clause 10 and of any publication policy described in the Protocol, provided any such policy does not obstruct publication unreasonably.
  2. Material for public dissemination will be submitted to the Sponsor for review at least thirty (30) days prior to submission for publication, public dissemination, or review by a publication committee. If Sponsor does not respond within this period, Site Parties are free to proceed with the intended publication or presentation without further delay.
  3. The Site Investigator and/or Research Staff agree that all reasonable scientific comments made by the Sponsor in relation to a proposed publication or presentation shall be considered for incorporation into the publication or presentation.
  4. During the period for review of a proposed publication referred to in clause 10.5 above, the Sponsor shall be entitled to
     1. make a reasoned request to the Site Investigator and/or Research Staff that publication be delayed for an additional period of sixty (60) days (following the thirty (30) day period referred to in clause 10.5 in order to enable the Sponsor to take steps to protect its proprietary information and/or Intellectual Property Rights and/or Know How and the Site Investigator and/or Research Staff shall not unreasonably withhold their consent to such a request; and
     2. cause the Site Investigator and/or Research Staff to remove from the intended publication any Sponsor Confidential Information received by Site Investigator that does not constitute results of the Clinical Study.

*Authorship and copyrights*

* 1. Publications will be in accordance with international recognized scientific and ethical standards concerning publications and authorship, including the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*, established by the International Committee of Medical Journal Editors. Copyrights concerning publications of the Clinical Study remain with the authors of the publication, regardless of any other provisions regarding intellectual property rights.

1. **TERM and TERMINATION**
   1. This Agreement commences on the Effective Date and shall continue in force until the earlier of:

a. completion of the Clinical Study, close-out of the Study Site and completion of the obligations of the Parties under this Agreement; or

b. early termination in accordance with clauses 11.2 or 11.3 of this Agreement;

11.2 Each Party may terminate this Agreement upon written notice to the other Parties with immediate effect in the following events only:

a. if the approval by the Ethics Committee is not granted or irrevocably revoked;

b. if it can be reasonably assumed that the Clinical Study must be terminated in the interests of the health of the Clinical Study Subjects;

c. if it becomes apparent, following confirmation of the Ethics Committee or the Independent Committee, that continuation of the Clinical Study cannot serve a scientific purpose;

d. if the Sponsor and/or the Study Site become or are declared insolvent or a petition in bankruptcy has been filed against it or if one of them is dissolved;

e. if circumstances beyond a Party’s control occur that render continuation of the Clinical Study unreasonable as outlined in clause 13;

f. if one of the Parties fails to comply with the obligations arising from the Agreement and, if capable of remedy, is not remedied within 30 days after receipt of written notice from the other Party specifying the non-compliance and requiring its remedy, unless the severity of the failure to comply does not reasonably justify the premature termination of the Clinical Study; or

g. if the Site Investigator is no longer able (for whatever reason) to act as investigator for this Clinical Study and no mutually acceptable replacement has been found in accordance with clause 2.3.

11.3 Sponsor may terminate this Agreement upon written notification to the Site Investigator and the Study Site with immediate effect, in the following events: a) for lack of recruitment at the Study Site, in case the Clinical Study is conducted at one site only; or

b) in case of a multicentre study, if termination at the Study Site does not affect performance of the Protocol.

The foregoing provided however, that this clause 11.3 shall not apply and Sponsor shall have no right to terminate this Agreement if any Clinical Study Subject has signed the ICF, at the Study Site.

11.4 At close-out of the Study Site following termination or expiration of this Agreement the Site Investigator and the Study Site shall, upon first request, immediately return to the Sponsor or destroy with confirmation thereof all Confidential Information, Equipment and/or unused materials or unused Study Drug and/or unused Investigational Product provided by Sponsor in accordance with Sponsor’s instructions, except for copies to be retained in order to comply with Site Parties’ archiving obligations or for evidential purposes.

1. **FINANCIAL PROVISIONS / STUDY DRUG / MATERIAL / EQUIPMENT**
   1. The Sponsor will provide [or A: no] reimbursement in support of the Clinical Study, [or B: solely if and to the extent as set out in Annex 2] [or C: in the amount of [insert amount] within 45 days after receipt of an invoice from the Study Site, including, when applicable, the rate of VAT in effect on the date of the invoice.
   2. [IF APPLICABLE: DESCRIBE WHAT STUDY DRUG / MATERIAL / EQUIPMENT IS PROVIDED AND HOW IT IS DELIVERED, REIMBURSED , ETC. – and/or in Annex 2 as well]
   3. Any arrangements with the pharmacy of Study Site to the extent applicable will be in writing and must be in accordance with the Site Parties’ internal policies, to the extent these are sufficiently communicated by the Site Parties. Any such agreements will be annexed to this Agreement.
   4. The Site Parties shall not use or permit the Research Staff or any third party to use the Study Drug, material or equipment for any purpose other than the conduct of the Clinical Study and upon termination or expiration of this Agreement all unused Study Drug, material or equipment shall, at the Sponsor’s option, either be returned to the Sponsor or disposed of in accordance with the Protocol or the Sponsor’s written instructions.
2. **FORCE MAJEURE**

13.1 No Party shall be liable to the other Parties or shall be in default of its obligations hereunder if such default is the result of war, hostilities, terrorist activity, revolution, civil commotion, strike, and epidemic or because of any other cause beyond the reasonable control of the Party affected. The Party affected by such circumstances shall promptly notify the other Parties in writing when such circumstances cause a delay or failure in performance and where they cease to do so.

1. **MISCELLANEOUS** 
   1. Parties shall have the right to assign this Agreement to an Affiliate upon prior written notification of the other Party/Parties, any other assignment shall take place upon the prior written approval of the other Party/Parties. Any approval by a Party of an assignment, transfer or encumbrance by the other Party shall not release the assigning Party of any of its obligations under this Agreement due up until such assignment. Subject to the foregoing, this Agreement shall bind and inure to the benefit of the respective Parties and their successors and assignees.
   2. Site Parties may not sub-contract the performance of all or any of their obligations under this Agreement without the prior written consent of the Sponsor, such consent not to be unreasonably withheld or delayed. Any Party who so sub-contracts shall be responsible for the acts and omissions of its sub-contractors as though they were its own.
   3. Nothing in this Agreement shall be construed as creating a joint venture, partnership or contract of employment between the Parties.
   4. Should there be any inconsistency between the Protocol and the terms of this Agreement, or any other document incorporated therein, the Protocol shall prevail in case such inconsistency concerns clinical matters and the Agreement shall prevail the inconsistency concerns non-clinical matters. For the avoidance of doubt, Termination and Publication provisions of this Agreement shall always prevail above the Protocol.
   5. The clauses 4 (Liabilities, Indemnification and Insurance); 6 (Quality Assurance and Control); 7.3-7.11 (Medical confidentiality, data protection and data controlling); 8 (Intellectual Property); 9 (Publicity); 10 (Publication and Authorship); 11.4 (Term and Termination); 12 (Financial Provisions/Study Drug/Material/Equipment); this clause 14.5 (Surviving Clauses); 14.6 (Governing Law); 15 (Human Samples) or other clauses contemplating performance after termination, shall survive termination or expiry of this Agreement. The provisions of clauses 7.1 and 7.2 (Confidential Information) shall remain in force for a period of five (5) years from the date of such termination or expiry.
   6. This Agreement shall be exclusively governed by, and construed in all respects in accordance with the laws of The Netherlands without regard to any of its conflicts of laws rules. Any claims, controversies or disputes arising out of or in connection with this Agreement which cannot be settled amicably between the Parties, shall be subject to the exclusive jurisdiction of the competent court in The Netherlands.
   7. Each person signing this Agreement represents and warrants that he or she is duly authorized and has legal capacity to execute and deliver this Agreement. Each Party represents and warrants to the other that the execution and delivery of the Agreement and the performance of such party's obligations hereunder have been duly authorized and that the Agreement is a valid and legal agreement binding on such party and enforceable in accordance with its terms.
2. **HUMAN SAMPLES**

15.1 As part of the Protocol, Samples derived from Clinical Study Subjects may be transferred to Sponsor or another organization indicated by Sponsor (hereinafter: “**Sponsor’s Designee**”), however only if this is arranged for in the ICF. If this done in non-anonymous form, Sponsor and Sponsor’s Designee shall adhere to the provisions of the GDPR by concluding an industry standard processor agreement with each other.

15.2 Sponsor, and if applicable Sponsor’s Designee, shall have the right to store, transfer and use the Samples only in accordance with the applicable Law (at least laws and regulations concerning the protection of privacy), the Protocol and ICF. Site Parties shall promptly notify Sponsor of any withdrawal of or changes in the informed consent of a Clinical Study Subject, which may affect the use of such Clinical Study Subject’s Samples under this Agreement. In such event, Sponsor or Sponsor’s Designee shall destroy, with written confirmation thereof, or return the affected Samples, where necessary and possible.

15.3 Upon termination or expiration of the Clinical Study, and at least at any time the Samples are no longer needed to be retained by Sponsor, or Sponsor’s Designee, for purposes defined in the ICF, or as required per any applicable Law or regulation, the remainder of the Samples in Sponsor’s or Sponsor’s Designee’s possession will be returned to the Site Parties, or retained by the Sponsor in accordance with clause 15.2 or destroyed by the Sponsor/Sponsor’s Designee, as described in the Protocol and/or the ICF, with written confirmation thereof.

15.4 For the avoidance of any doubt, the control *(*in Dutch: “zeggenschap”*)* of the Samples remains at all times with the Clinical Study Subjects they are derived from, while the Site Parties and/or Sponsor are acting as custodian of the Samples, as described in the Protocol.

1. **Conditional Approval**
   1. This agreement is signed and entered into under the condition that recruitment and/or inclusion of Study Subjects will not start until the Ethics Committee has granted approval for the Protocol as submitted on to the Ethics Committee.
   2. Either Party may terminate this Agreement in accordance with clause 11 in case the Ethics Committee;

a. withholds its approval of the Protocol as submitted to the Ethics Committee;

b. makes its approval subject to modification(s) of the Protocol that requires amendment(s) of the Verklaring Geschiktheid Onderzoeksinstelling (“VGO”) [Declaration Feasibility Site] and/or the Agreement.

Annexes

Annex 1: Protocol

Annex 2: Financial Provisions/ Study Drug / Material / Equipment (if applicable)

Annex 3: Funding Conditions (if applicable)

Annex 4: Template Monitoring Letter

*[The remainder of this page is intentionally left blank]*

Signed on behalf of the **Sponsor**

Signature: …………………………………………

Name: …………………………………………

Title: …………………………………………

Date: …………………………………………

Signed on behalf of the **Study Site**

Signature: …………………………………………

Name: ……………………………

Title: ……………………………

Date: …………………………………………

[N.B. In case a “medisch specialistisch bedrijf” will cosign the Agreement: insert signature field for

Signed on behalf of the **MSB …………**

Signature: …………………………………………

Name: ……………………………

Title: ……………………………

Date: …………………………………………

*[***if the Site Investigator is NOT a contracting Party insert:** *The undersigned Site Investigator hereby declares that he/she has read the above Agreement between the Parties and that he/she acknowledges the provisions of the Agreement relative to his/her role, responsibilities and duties concerning the Clinical Study;]*

Signed by the **Site Investigator:**

Signature: …………………………………………

Name: ……………………………

Title: ……………………………

Date: …………………………………………

ANNEX 1

**PROTOCOL**

(*the most recent version of the Protocol has been incorporated* *by reference only*)

ANNEX 2 **(if applicable)**

**FINANCIAL PROVISIONS / STUDY DRUG / MATERIAL / EQUIPMENT**

ANNEX 3**(if applicable)**

**FUNDING CONDITIONS**

ANNEX 4

**Template Letter Study Monitor**

Ziekenhuis naam (Study Site)

Adres

Postcode en plaats

[plaatsnaam Sponsor], [datum]

**Betreft: Opdracht monitoren klinische studie**

Geachte heer/mevrouw,

[naam Study Site] doet mee aan het ondergenoemde klinische onderzoek. Zoals bepaald in de Clinical Study Agreement over dit onderzoek is [naam Sponsor] verantwoordelijk voor monitoring. Namens [naam Sponsor] zal [naam monitor] (hierna “**Monitor**”) regelmatig in uw ziekenhuis aanwezig zijn om de studiedata te monitoren. Deze Monitor zal in overeenstemming met Good Clinical Practice (GCP) en/of ISO14155, het contract en het studieprotocol de studiedata aan de hand van de brondata verifiëren.

Monitor zal vertrouwelijk omgaan met alle gegevens die hij/zij inziet en Sponsor verklaart hierbij dat Monitor een geheimhoudingsverklaring heeft getekend.

Monitor heeft de volgende faciliteiten nodig van het ziekenhuis om te kunnen monitoren:

* toegang tot alle patiënten data, waaronder het elektronisch patiëntendossier (EPD) van de patiënten die deelnemen aan ondergenoemde klinische studie.
* Monitor heeft alleen een controlefunctie, derhalve heeft zij enkel recht op inzage in het EPD en geen schrijfrecht.
* Dit inzagerecht is daarbij beperkt tot de patiënten die deelnemen aan de ondergenoemde studie.

**Naam studie:**

**Studie id:**

**Protocol nummer:**

Deze verklaring geldt voor de duur van de studie en alleen voor de genoemde Monitor.

Met vriendelijke groet,

[naam tekenbevoegde] Raad van Bestuur [naam Sponsor]